REMARKS

Applicant notes with appreciation the thoroughness of the Office Action as detailed in Paper 20070502. This response is submitted to be fully responsive thereto.

Currently claims 1, 3-12, 15-19, 21-28, and 39 are pending in the application.

Claims 1, 3, 7-9, 11, 12, 15-19, 21, 24-26 and 28 are rejected under 35 U.S.C. §102(e) over Korlach et al. (U.S. 7,056,676).

Claims 4, 6, 10, 23, 27 and 39 are rejected under 35 U.S.C. §103(a) as being unpatentable over Korlach et al. (U.S. 7,056,676) in view of Kambara et al. (U.S. 5,824,481).

Additionally claims 5 and 22 are rejected under 35 U.S.C. §103(a) over Korlach et al. (US. 7,056,676) in view of Montgomery (U.S. 6,444,111).

Remarks Directed to Claim Rejections under 35 U.S.C. §102(e) to Claims 1, 3, 7-9, 11, 12, 15-19, 21, 24-26 and 28 over Korlach et al., U.S. Patent No. 7,056,676

As stated on pages 2-3 of the Paper No. 20070502, Korlach et al. discloses "sequencing nucleic acid via primer extension reactions wherein a labeled nucleotide is incorporated into a nascent strand" with the use of "a variety of fluorescent moieties including metals"; performing polymerase chain reaction; "performing fluorescence resonance energy transfer", and performing "serial detection of nucleotides that are incorporated into the growing strand."

For the reasons stated below, Applicant submits that the pending claims are not anticipated by Korlach et al.

Independent claims 1 and 15 each recite a process comprising "providing" a labeled oligonucleotide and "assaying for the labeled oligonucleotide", whereas the labeled oligonucleotide is "characterized by an association *independent* of a dual contribution covalent bond between the detectable moiety and the oligonucleotide." (Emphasis Added).

Korlach et al. discloses nucleotide labeling with fluorophor (pages 2-3 of the Paper 20070502) via a covalent bond. Korlach et al. does not teach or even indicate the desirability of labeling via a bond that is not a dual contribution covalent bond.

The association characterized as such by claim 1 or 15 is described in further detail at page 6, lines 2-8 of the specification. As described, an association independent of a dual contribution covalent bond illustratively includes formation of an ionic bond, a hydrogen bond, Van der Waals interaction, or an organometallic bond. It is known that a conventional dual contribution covalent bond occurs when two atoms share electrons in the bond. A non-covalent bond, on the other hand, differs both in bond structure and bond strength with a conventional dual contribution covalent bond.

In comparison to a conventional covalent bond which is very stable, if not too rigid, a coordinate bond such as in the case of the ULYSIS reagent of the Example 1 is much more flexible and provides a different energy transfer profile for exciting the fluorophor signal.

Therefore, as analyzed above, Korlach et al. fails to disclose labeling an oligonucleotide through a bond that is independent of a dual contribution covalent bond, as recited in independent claims 1 or 15.

Furthermore, Korlach et al. fails to teach the claimed elements of associating a detectable moiety directly onto an oligonucleotide or the detection of such labeled oligonucleotide.

Furthermore, unlike the instant invention where a labeled oligonucleotide is detected in the context of oligonucleotide elongation, Korlach et al. teaches the detection of single base nucleotide in the context of nucleic acid sequencing.

As such, Korlach et al. fails to disclose or teach at least one element of independent claims 1 or 15. The subject matter of independent claims 1 and 15 and claims dependent

therefrom is therefore entitled to patentable weight. Reconsideration and withdrawal of the rejections to claims 1, 3, 7-9, 11-12, 15-19, 21, 24-26, and 28 under 35 U.S.C. §102(e) over Korlach et al. is requested.

Remarks Directed to Rejections to Claims 4, 6, 10, 23, 27 and 39 under 35 U.S.C. §103(a) as Being Unpatentable over Korlach et al. (U.S. 7,056,676) in View of Kambara et al. (U.S. 5,824,481)

Applicant incorporates by reference the above remarks regarding §102 rejections over Korlach et al. As claims 4, 6, 10, 23 and 27 depend from claims 1 and 15, now believed to be in allowable form, these claims dependent therefrom respectively are likewise submitted to be allowable.

It is stated on page 4 of the Paper 20070502 that Korlach et al. "does not identify fluorescent compounds that comprise a metal, nor the use of ligase" and "It would have been obvious to one of ordinary skill in the art to substitute alternative labels and enzymes in the method of Korlach et al., as disclosed by Kambara et al."

Applicant submits that the pending claims are patentable as the claims are not obvious over Korlach et al. and Kambara et al. for the additional reasons stated below.

Korlach et al. teaches, as noted above, the use of labeled nucleotide analogs in a polymerization reaction so as to perform nucleic acid sequencing. However, Korlach et al. fails to teach or suggest that an oligonucleotide is pre-labeled with a detectable moiety; or that labeling is through an association independent of a conventional dual contribution covalent bond; or that the labeled oligonucleotide is detected as reflecting elongation event.

Kambara et al. fails to bolster the deficiency of the teachings of Korlach et al. Kambara et al. discloses an alternative approach to accomplish direct sequencing DNA molecules that are of megabases in length (column 5 lines 22-27). In so doing Kambara et al. teaches fragmentation

of the long DNA molecules into DNA fragments of manageable sizes, typically of several thousand bases long (column 5, lines 26-28). Because of the intended operation of Kambara et al. with regard to fragmenting and sequencing long DNA molecules, the resulting DNA fragments are labeled merely to "ensure that many types of the generated DNA fragments can be easily separated and isolated (FIG.2)" (column 2 lines 46-50). Nowhere does Kambara et al. teach the presence of labeled DNA fragments as corresponding to an elongation event.

As such, Korlach et al. and Kambara et al., alone or in combination, fail to teach or suggest that an oligonucleotide is pre-labeled with a detectable moiety or a fluorescence compound; or that labeling is through an association independent of a traditional dual contribution covalent bond, or that the labeled oligonucleotide is detected as reflecting elongation event.

Further, if those several thousand base long labeled DNA fragments of Kambara et al. are to replace the single base nucleotide analog of Korlach et al., no sequence will be deciphered; in fact, no sequencing reaction may even be possibly initiated. Therefore the intended operation of Korlach et al. will be destroyed if the teachings of Kambara et al. as to labeling are combined with the teachings of Korlach et al. as to DNA sequencing. See *In re Gordon*, 773 F.2d 900; 221 USPQ 1125 (Fed. Cir. 1984).

In light of these remarks, reconsideration and withdrawal of rejections to claims 4, 6, 10, 23, 27, and 39 under 35 U.S.C. §103(a) over Korlach et al. in view of Kambara et al. is requested.

Remarks Directed to Rejections to Claims 5 and 22 under 35 U.S.C. §103(a) over Korlach et al. (U.S. 7,056,676) in View of Montgomery (U.S. 6,444,111)

Applicant incorporates by reference the above remarks directed to Korlach et al. with regard to rejections under 35 U.S.C. §102(e) and §103(a).

It is stated on pages 4-5 of the Paper 20070502 that "Korlach et al. has not been found to disclose the use of fluorescence in conjunction with platinum" and Montgomery is cited to bolster the limitation of Korlach et al. since Montgomery is cited to have disclosed platinum as a quencher of unwanted unintentional fluorescence and "It would have been obvious to one of ordinary skill in the art to have modified the method of Korlach et al. so as to incorporate the presence of platinum of Montgomery as such would have allowed the artisan to readily quench any unwanted fluorescence, thereby increasing the sensitivity and accuracy of the assay."

Applicant submits, for the reasons stated below, that claims 5 and 22 are not obvious over Korlach et al. in view of Montgomery.

As noted above, Korlach et al. fails to teach or suggest the subject matter of independent claims 1 or 15, specifically that an oligonucleotide is pre-labeled with a detectable moiety; or that labeling is through an association independent of a conventional dual contribution covalent bond; or that the labeled oligonucleotide is detected as reflecting elongation event.

Montgomery fails to bolster the above mentioned deficient teachings of Korlach et al. As such, it is submitted that subject matter of independent claim 1 or claim 15 is entitled to patentable weight.

Furthermore, for the reasons stated below, Applicant submits that Korlach et al. and Montgomery, alone or in combination, also fails to teach the subject matter of claim 5 or 22

either of which recites an oligonucleotide labeled with a metal containing fluorescent wherein the metal is platinum.

Montgomery fails to bolster the deficient teaching of Korlach et al. as to labeling an oligonucleotide with a metal containing fluorescence wherein the metal is platinum. In fact, Montgomery teaches away for the use of platinum as a way of introducing fluorescence per the instant invention since Montgomery clearly teaches the use of platinum to quench a fluorescent signal (pages 4-5 of the Paper 20070502). In Montgomery, platinum is used rather as a building material to construct electrodes (column 7, lines 63-65). A fluorescent membrane is applied to and overlays the platinum electrodes (column 8, lines 2-5). When the platinum material in the electrodes is darkened, it causes quenching of the fluorescence in the fluorescent membrane (column 7, lines 63-65). Nowhere does Montgomery disclose or suggest labeling of an oligonucleotide, let alone labeling of an oligonucleotide with a metal containing fluorescence wherein the metal is platinum. Montgomery teaches, quite on the contrary, the quenching of fluorescence by the use of platinum is the substantive teaching therein.

It is further noted that the contention "it would have been obvious ... so to incorporate the presence of platinum ... to readily quench any unwanted fluorescence, thereby increasing the sensitivity and accuracy of the assay" (page 5 of the Paper 20070502) is an incorrect reading of the pending claims. As noted above, the fluorescence indicated in claims 5 or 22 of the instant invention is not to be quenched but rather to be wanted, let alone increasing sensitivity by quenching fluorescence by the use of platinum. In fact, as noted above, the instant invention rather recites a process where fluorescence is introduced through the use of platinum binding moiety to the oligonucleotide.

Korlach et al. and Montgomery, alone or in combination, fails to teach or even provide suggestion as to labeling an oligonucleotide, let alone labeling the oligonucleotide with a metal containing fluorescence wherein the metal is platinum. The subject matter of claims 5 and 22 is therefore entitled to patentable weight. Reconsideration and withdrawal of rejections to claims 5 and 22 under 35 U.S.C. §103(a) over Korlach et al. in view of Montgomery is requested.

Summary

Claims 1, 3-12, 15-19, 21-28, and 39 are the pending claims in this application. Each claim is believed to be in proper form and directed to allowable and patentable subject matter. Reconsideration and allowance of the claims is requested. The Examiner is kindly requested to contact the undersigned attorney in charge of this application in the event that issues remain after consideration of this response.

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Respectfully submitted,

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